UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/762,873	01/21/2004	Nicholas M. Valiante	PP20203.0003	5927

27476 7590 10/06/2008

NOVARTIS VACCINES AND DIAGNOSTICS INC.
INTELLECTUAL PROPERTY R338
P.O. BOX 8097
Emeryville, CA 94662-8097

EXAMINER	
CHONG, YONG SOO	
ART UNIT	**PAPER NUMBER**
1617	

MAIL DATE	DELIVERY MODE
10/06/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/762,873	VALIANTE, NICHOLAS M.	
	Examiner	Art Unit	
	YONG S. CHONG	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 July 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *1-11,18 and 20-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12-17, 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

This Office Action is in response to applicant's arguments filed on 7/25/08. Claims 23-31 have been cancelled. Claims 1-22 are pending. Claims 1, 3, 12 have been amended. Claims 1-11, 18, 20-22 have been withdrawn. Claims 12-17, 19 are examined herein.

Applicant's arguments have been fully considered but found not persuasive. The 103(a) rejection of the last Office Action is maintained for reasons of record and repeated below for Applicant's convenience.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham vs John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 12-17, 19 are rejected under 35 U.S.C. 103(a) as being obvious over Baker et al. (US Patent 5,441,955) in view of Colston et al. (US Patent 7,122,195 B2).

The instant claims are directed to a composition comprising a tryptanthrin compound (No. 1001) and an antigen.

Baker et al. teach the tryptanthrin compound of No. 1001 in the applicant's specification (col. 20, lines 22-33) as part of an antimicrobial composition (abstract). Furthermore, this tryptanthrin compound can be administered with an adjuvant (col. 12, lines 37-42). What's more, Baker et al. teach that tryptanthrin can be administered in combination with one or more other agents used in the treatment of pathogenic mycobacterial infections. Representative agents used for the treatment of mycobacterial tuberculosis include, for example, isoniazid, rifampin, pyrazinamide, ethambutol, rifabutin, streptomycin, and ciproflaxin (col. 13, lines 35-43). Examiner would like to point out that mycobacterial tuberculosis is a common cause of bacterial meningitis (meningococcus infection). Moreover, Bacillus of Calmette and Guérin (BCG) is a vaccine against tuberculosis caused by mycobacterial tuberculosis.

Examiner reminds Applicant that the limitation "for enhancing an immune response" in claim 12 is considered preamble or intended use, since the claims are drawn to a composition, therefore will given little patentable weight.

It is respectfully pointed out that a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish from each other. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a

process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). Thus, the intended use of a composition claim will be given no patentable weight.

It is further respectfully pointed out that a preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951). See MPEP 2111.02.

Examiner further reminds Applicant that the limitations “immunogenic” and “providing an enhanced immune response to the antigen than provided without the tryptanthrin compound adjuvant" in claim 12 as well as “enhances an immune response to the antigen and the immune response is the cellular production of one or more cytokines” in claim 15 will be given little patentable weight since a composition and its properties are inseparable.

“Products of identical chemical composition can not have mutual exclusive properties.” Any properties exhibited by or benefits from are not given any patentable weight over the prior art provided the composition is inherent. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the disclosed properties are necessarily present. *In re Spada*, 911 F.2d 705, 709, 15 USPQ 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01. The

burden is shifted to the applicant to show that the prior art product does not inherently possess the same properties as the instantly claimed product.

Baker et al., however fails to disclose a specific combination of the tryptanthrin compound (No. 1001) and an antigen disclosed in claim 14.

Colston et al. teach that recA mutant mycobacteria, particularly mutants of mycobacterial species which are members of Mycobacterium tuberculosis, are useful as vaccines for the treatment of a range of disorders, including tuberculosis (abstract). Colston et al. teach that this invention may be used as an antigen delivery system in the treatment of any disease, such as pathogenic infection, which is ameliorated by an immune response against a particular antigen. Suitable antigens include viral, protozoal, tumour cell, bacterial, and fungal antigens, for example an antigen from the Tetanustoxin, and Diphtheriatoxin. Such an antigen may be useful in the treatment of tetanus and diphtheria (col. 4, line 51 to col. 5, line 14).

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed invention was made, to combine the tryptanthrin compound (No. 1001) as disclosed by Baker et al. with the composition comprising antigens associated with tetanus or diphtheria as disclosed by Colston et al.

A person of ordinary skill in the art would have been motivated to combine the tryptanthrin compound (No. 1001) with a composition comprising antigens associated with tetanus or diphtheria because: (1) both Baker and Colston are analogous are since both teach the treatment of pathogenic mycobacterial infections, for example tuberculosis; (2) Baker teaches that the tryptanthrin compound can be administered with

an adjuvant or another agent used in the treatment of pathogenic mycobacterial infections; (3) Baker teaches the use of antigens such as BCG in a vaccine against tuberculosis; (4) Colston teaches an antigen delivery system in the treatment of any disease, such as pathogenic infection, which is ameliorated by an immune response against a particular antigen; and (5) Colston specifically discloses suitable antigens, such as include viral, protozoal, tumour cell, bacterial, and fungal antigens, for example antigens from the Tetanustoxin and Diphtheriatoxin.

"It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... The idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

Response to Arguments

Applicant argues that the prior art does not disclose the claimed composition, therefore the claimed properties are not present in the prior art. The compounds of Formula I were at least partially known because they were not known to be mixed with an antigen. Therefore, the limitation "to provide an enhanced immune response to the antigen relative to the response provided without the tryptanthrin compound adjuvant" should be afforded patentable weight. This phrase limits the composition in a substantive way, though it does so using a functional limitation.

This is not persuasive because the claimed composition is disclosed by the cited prior art. Applicant is reminded that the obviousness rejection is based on the combination of two prior art references, which must be considered together. In response to applicant's arguments against the references, one cannot show nonobviousness by attacking references individually where the rejections are based on the combination of references. See *In re Keller*, 642 F. 2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F. 2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Since the cited prior art discloses all components in the prior art, the limitations drawn to the properties of the composition is inherent. Applicant is invited to show factual data showing that the composition rendered obvious by the cited prior art does not possess the same functional properties of the claimed composition.

Applicant argues that since drug interactions are common, one does not casually combine drugs merely because they are known in a general sense to be useful for treating a particular type of condition. Applicant submits Exhibit A to show that the user of BCG is specifically advised to tell her doctor if she is using antibiotics, which suggests that drug interactions with antibiotics are a concern for a user of BCG. Applicant also argues that it would not be obvious to combine the two into a single composition because vaccines are typically administered once, whereas antibacterials are typically administered over a period of days and in many doses.

This is not persuasive because this line of reasoning is applicable to any combination of drugs. Naturally, this is a general concern for anyone in the medical field, however nothing in Exhibit A states that BCG cannot be combined with another

active agent, let alone a compound of Formula I. In fact, nothing is even said about drug to drug interactions in Exhibit A. Furthermore, Applicant's arguments directed to the number of doses are not persuasive because even a single dose of an antibacterial compound along with a single vaccine would be enough to render the claimed composition obvious. In other words, there is nothing in the claims to preclude the further administration of the same antibacterial minus the vaccine since the claims use the open transitional language “comprising.”

Applicant argues that the combination of the antibacterial of Baker and the vaccine of Colston would be expected to be ineffective, since the antibacterial compound would be expected to kill the vaccine's active cells. Thus it would not be logical to administer BCG along with an antibacterial like the compounds of Formula I because the antibacterial would be expected to harm the bacteria in the vaccine or in the treated patient.

This is not persuasive because Applicant is arguing against their own claimed invention. If the composition comprising the combination of the cited prior art is ineffective, why is it that the same composition claimed by the Applicant be enabled?

Applicant argues against using Kerkhoven case law because this case is an entirely different situation. The compositions in this case are not merely two conventional cleaning agents that one might casually mix together. Here, one of the compositions is an antibacterial compound, which acts by killing a bacterium, according to Baker. The other is a vaccine composition that acts by a completely different mechanism, eliciting an immune response. Thus, the two materials require different

formulations, different administration schedules, and different storage conditions as well as have different effects, purposes, and are suitable for use in different patients.

This is not persuasive because while these differences may or may not be true, the fact remains that Baker discloses these two active agents for the treatment of pathogenic mycobacterial infections. Baker also teaches that tryptanthrin can be administered in combination with one or more agents or adjuvants. Applicant is also reminded that there are many combination therapies in the medical field that work via different or multiple mechanisms of action. Therefore, one of ordinary skill in the art would have had a reasonable expectation of success in treating pathogenic mycobacterial infections by administering tryptanthrin with an adjuvant because of the therapeutically additive effect of combining two known active agents for the same purpose.

Applicant argues that Colston uses mycobacterium as a living cell along with an antigen, which is the essential part of what Colston says is effective for treating an infection. However, the compounds of Baker are useful for treating infections because they kill bacteria. Because Colston uses live bacteria and Baker's compounds kill bacteria, it would not be appropriate to mix those cells with compounds from Baker. Moreover, Exhibit B is submitted to show interactions between vaccine compositions and antibiotics. It demonstrates that vaccines are often antagonized (made less effective) by antibiotics, so it was not predictable that mixing an antibacterial compound of Baker with an antigenic composition would work, prior to the present invention.

This is not persuasive because since the methods disclosed by the cited prior art are for treating mycobacterial infections, the antigen disclosed by Colston will come into contact with a mycobacterium in the infected patient so that work as intended. Again, the argument against Baker's teaching that the disclosed compounds will kill the bacteria is not persuasive because it is Applicant's burden to show factual data that the composition disclosed by the cited prior art will not work for its intended use. Moreover, this line of reasoning is directly challenging Applicant's claimed invention. Applicant is requested to explain and show factual data that the claimed antibacterial compounds will not kill the mycobacterium that is needed for the adjuvant to work as intended.

In regards to Exhibit B, the reference does not state that the combination of vaccines and antibiotics will not work, but that the combination will be less effective. Nonetheless, the reference says nothing about the particular combination cited by the prior art or the claimed invention. Applicant is reminded that the standard for obviousness is not absolute but a reasonable expectation of success.

Applicant argues against a case of obviousness by claiming unexpected results in the form of the immunogenic effect of an antigen as enhanced by a compound of Formula I.

The Valiante Declaration under 37 CFR 1.132 filed 10/31/2007 is insufficient to overcome the rejection of claims 12-17, 19 based upon Baker et al. (US Patent 5,441,955) in view of Colston et al. (US Patent 7,122,195 B2).

It include(s) statements which amount to an affirmation that the claimed subject matter functions as it was intended to function. This is not relevant to the issue of

nonobviousness of the claimed subject matter and provides no objective evidence thereof. See MPEP § 716.

The Valiante Declaration simply states that the tryptanthrin compound can be effective in generating an immune response as viewed in Table 1. The ability to stimulate TNF-alpha production is viewed as unexpected based on previously known properties of tryptanthrin. Examiner does not view this as unexpected properties since tryptanthrin is a known compound. Furthermore, the claims and rejection are based on the combination of tryptanthrin compound and an antigen in claim 14. There is no factual data, commensurate with the scope of the claims to overcome a prima facie case of obviousness.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong S. Chong whose telephone number is (571)-272-8513. The examiner can normally be reached on M-F, 9-6.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, SREENI PADMANABHAN can be reached on (571)-272-0629. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Yong S Chong/
Examiner, Art Unit 1617

YSC